NAME: Ceglia, Lisa

eRA COMMONS USER NAME: LCEGLIA144

POSITION TITLE: Associate Professor of Medicine; Scientist II at the Human Nutrition Center

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Harvard University	B.A.	06/1993	Fine Arts
New York University School of Medicine	M.D.	06/2001	Medicine
New York University/Bellevue Medical Center	Post-Doctoral	06/2004	Residency, Medicine
Tufts Medical Center	Post-Doctoral	06/2007	Fellowship, Endocrinology
Jean Mayer USDA Human Nutrition Research Center on Aging (HNRCA) at Tufts University	Post-Doctoral	06/2009	Fellowship, Human Nutrition
Tufts School of Graduate Biomedical Sciences	M.S.	06/2011	Clinical & Translational Science

A. Personal Statement

I am an endocrinologist with expertise in osteoporosis, sarcopenia, and nutrition. I have received formal training in clinical research as a KL2 awardee at Tufts CTSI, and specific training in the areas of bone and muscle health and aging under a career development award at the Boston Claude Pepper Older Americans Independence Center. I currently serve as the Director of the Metabolic Bone Diseases Clinic at Tufts Medical Center and actively treat patients with bone and mineral disorders. I also serve as the Director of the Metabolic Research Unit at the Tufts University Jean Mayer USDA Human Nutrition Research Center on Aging where I conduct my own clinical research, and also oversee the safety of all human research. Through my research activities for over 10 years as an independent investigator implementing and leading interventional studies on musculoskeletal health in older adults, I have accumulated further knowledge and experience in clinical research in the areas of nutrition and metabolic disease.

Ongoing and recently completed projects that I would like to highlight include: U01 DK098245 Pittas (PI) 06/01/13 - 05/31/22 (NCE) Vitamin D and type 2 diabetes (D2d) study Role: Co-Investigator

5R01AG055443 Ceglia (PI) 09/30/18-02/29/24 NIH/NIA Impact of protein and alkali supplementation on skeletal muscle in older adults

5R21AR074138 Dawson-Hughes (PI) 04/10/19-02/28/22 NIH/NIAMS Effect of a ghrelin receptor agonist on muscle and bone Role: Co-investigator BIO101-CL03 Biophytis S.A./ICON Fielding (PI) 07/16/18-07/31/21 Safety and Efficacy of BIO-101 175 mg b.i.d. and 350 mg b.i.d. 26-week oral administration to patients suffering from age-related SARcopenia, including sarcopenic obesity, Aged >65 years and at risk of mobility disability. A double-blind, placebo controlled, randomized INTerventional Clinical Trial Role: Co-Investigator

Lonza Work Order #2 Fielding (PI) 07/01/16-02/28/21 Lonza Therapeutic Role of L-Carnitine and Creatine in Skeletal Muscle Hypertrophy Role: Co-Investigator

DSM Nutritional Products AG Ceglia (PI) 11/01/13-12/31/19 25(OH)D supplementation in younger postmenopausal women Role: Co-Investigator

- Pittas AG, Dawson-Hughes B, Sheehan PR, Ware MS, Knowler WC, Aroda VR, Brodsky I, Ceglia L et al. Vitamin D supplementation and prevention of type 2 diabetes. NEJM. 2019: 381:520-530. PMCID: <u>PMC6993875</u>
- Ceglia L, Nelson J, Ware J, Alysandratos KD, Bray GA, Garganta C, Nathan DM, Hu FB, Dawson-Hughes B and Pittas AG. Association between body weight and composition and plasma 25-hydroxyvitamin D level in the Diabetes Prevention Program. *Eur J Nutr.* 2017 Feb; 56(1):161-170 [PMID26525562]
- 3. **Ceglia L**, Harris SS, Abrams SA, Rasmussen HM, Dallal GE, **Dawson-Hughes B**. (2009) Potassium bicarbonate attenuates the urinary nitrogen excretion that accompanies an increase in dietary protein and may promote calcium absorption. *J Clin Endocrinol Metab*, 94(2):645-53. PMCID: PMC2730228.
- Ceglia L, Dawson-Hughes B. Increasing alkali supplementation decreases urinary nitrogen excretion when adjusted for same day nitrogen intake. Osteoporosis Int, 2017 Dec; 28(12): 3355-3359. PMCID: PMC6592622.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

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Director, Endocrinology Clinic, Division of Endocrinology, Tufts Medical Center, Boston, MA
Associate Professor, Tufts University School of Medicine, Boston, MA
Expert Grant Reviewer, Tufts CTSI Center Pilot Program Grants
Laboratory Director of the Nutritional Evaluation Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA
Medical Director of the Metabolic Research Unit at the Jean Mayer USDA Human Nutrition
Research Center on Aging at Tufts University, Boston, MA
Scientist II, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University,
Boston, MA
External Expert Grant Reviewer (grant applications), Wellcome Trust (Physiological Sciences), United Kingdom; Boston Pepper Center Pilot Program Grants; Department of Veterans Affairs Cooperative Studies Program; TI Food and Nutrition, Netherlands
Assistant Professor, Tufts University School of Medicine, Boston, MA
Adjunct Scientist III, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA
Director of the Metabolic Bone Disease Clinic, Tufts Medical Center, Boston, MA Ad hoc reviewer, Journal of Bone and Mineral Research, Journal of Clinical Endocrinology and Metabolism, Osteoporosis International, Calcified Tissue International, Journal of Gerontology,

2007- 2007- 2007- 2006- 2005- 2004-2014 1995-1997 1992-1995	Clinical Endocrinology, Diabetologia, Medicine and Science in Sports and Exercise, Journal of Nutrition, Health and Aging, American Journal of Applied Physiology Attending Physician, Division of Endocrinology, Tufts Medical Center, Boston, MA Diplomate in Endocrinology, Diabetes and Metabolism (American Board of Internal Medicine) Member, American Society for Bone and Mineral Research Member, Endocrine Society Member, Massachusetts Medical Society Diplomate in Internal Medicine (American Board of Internal Medicine) Research Assistant, Dept. of Child and Adolescent Psychiatry (Dr. Cynthia R. Pfeffer) at New York Hospital-Cornell, White Plains, NY Research Assistant, Dept. of Addiction Services (Dr. David Gastfriend), Massachusetts General Hospital, Boston, MA
Honors 2018 2013 2012 2012-2013 2009-2011 2008-2010 2006-2009 2004-2006 2001 1993 1993	Research Career Development Forum Award Pilot grant, Jean Mayer Human Nutrition Research Center on Aging at Tufts University Honorary Member, Society of Medicine and Natural Sciences at the University of Parma The Dr. Gerald J. & Dorothy R. Friedman Foundation Junior Faculty Scholar Award KL2 Tufts CTSI Research Career Development Award Research Career Development Core Award, Pepper Older Americans Independence Center Post-Doctoral Fellow in Nutrition and Metabolism at Tufts University The Dr. Gerald J. & Dorothy R. Friedman Foundation Scholar Annual Humanism in Medicine Award, New York University School of Medicine John Harvard Scholarship Award Elizabeth Cary Agassiz Merit Award

C. Contributions to Science

- 1. *Alkali Supplementation and Skeletal Muscle. --* In a secondary analysis of the calcium and vitamin D supplementation trial STOP-IT, we found that alkalinogenic diets were associated with better lean tissue mass by dual energy X-ray absorptiometry in older men and women. Using an aging rat model, we also found that a net alkali-producing dietary load resulting from potassium bicarbonate (KHCO₃) supplementation led to more than 35% lower urinary nitrogen-to-creatinine ratio as compared to no supplementation with similar net acid load of typical modern diets. This finding was independent of vitamin D status. I served as the principal investigator in this study. I also served as principal investigator on a secondary analysis of our KHCO₃ dose-finding randomized placebo controlled trial for which we examined whether KHCO₃ altered serum microRNAs associated with bone and skeletal muscle function. This post-hoc study demonstrated that reducing renal acid load with KHCO₃ was associated with increased expressions of c-miR-133b and c-miR-21-5p. Furthermore, increases in c-miRNA-133b and c-miR-21-5p were inversely associated with bone resorption markers UNTX and UCa consistent with potential beneficial effects on bone in older adults. Finally in a recent pilot study, we found that potassium bicarbonate supplementation, by way of alkalinizing an energy-restricted diet in weight loss, may have beneficial effects on markers of muscle metabolism.
 - a. Dawson-Hughes B, Harris SS, **Ceglia L**. Alkaline diets favor lean tissue mass in older adults. *Am J Clin Nut* 2008 87: 662-665. PMCID: PMC2597402
 - b. Ceglia L, Rivas DA, Pojednic RM, Price LL, Harris SS, Smith D, Fielding RA, Dawson-Hughes B. (2013) Effects of alkali supplementation and vitamin D insufficiency on rat skeletal muscle. *Endocrine*, 44(2):454-464. PMCID: PMC4435679.
 - c. Margolis LM, Dawson-Hughes B, Rivas DA, Ezzyat Y, Fielding RA, Ceglia L. Effects of Potassium Bicarbonate Supplements on Circulating microRNA Expression. J Endo Soc. 2017 Jun 14;1(8):1015-1026.
 - d. Margolis LM, Ceglia L, Rivas DA, Dawson-Hughes B, Fielding RA. Pilot study examining the influence of potassium bicarbonate supplementation on nitrogen balance and whole-body ammonia and urea turnover following short-term energy restriction in older men. *Nutrients*. 2018 May 16;10(5): pii E624. PMCID: PMC5986503.

- 2. Vitamin D and Skeletal Muscle: -- I led an observational study that examined whether vitamin D status predicted muscle-related outcomes in a healthy adult male population. Our analysis found that there was no association between serum 25-hydroxyvitamin D concentration and lean body mass, muscle strength, or physical function after controlling for multiple health and lifestyle factors in a younger diverse sample of adult men. I led a randomized placebo controlled trial to study the impact of supplementation with vitamin D₃ 4000 IU/day on muscle microanatomy, strength and performance in older mobility-limited women with baseline vitamin D insufficiency. Vitamin D₃ supplementation for 4 months increased intramyonuclear vitamin D receptor concentration and muscle fiber size compared to placebo; however, we found no significant differences in strength and performance. I served as principal investigator or co-investigator in all of these studies.
 - a. **Ceglia L**, Chiu G, Harris SS, Aruajo A. (2011) Serum 25-hydroxyvitamin D concentration and physical function in adult men. *Clin Endocrinol (Oxf)*, 74(3):370-6. PMCID: PMC3066063.
 - b. Ceglia L, Niramitmahapanya S, Morais MD, Rivas DA, Harris SS, Bischoff-Ferrari H, Fielding RA, Dawson-Hughes B. (2013) A randomized study on the effect of vitamin D₃ supplementation on skeletal muscle morphology and vitamin D receptor concentration in older women. *J Clin Endocrinol Metab*, 98(12):E1927-35. PMCID: PMC3849671.
 - c. Pojednic RM, Ceglia L, Olsson K, Gustafsson T, Lichtenstein AH, Dawson-Hughes B, Fielding RA. (2015) Effects of 1,25-dihydroxyvitamin D₃ and vitamin D₃ on the expression of the vitamin D receptor in human skeletal muscle cells. *Calcif Tissue Int*, 96(3):256-63. PMCID: PMC4429607.
 - d. Pojednic RM, **Ceglia L**, Lichtenstein AH, Dawson-Hughes B, Fielding RA. (2015) Vitamin D receptor protein is associated with interleukin-6 in human skeletal muscle. *Endocrine*, 49(2):512-20. PMCID: PMC4447580.
- 3. **Vitamin D and Diabetes:** --I was a co-investigator and site PI on the Vitamin D supplementation and Prevention of Type 2 Diabetes multicenter trial which found no significant effect of 4000 IU/day of vitamin D₃ (vs. placebo) on risk of developing type 2 diabetes among adults with prediabetes. I am currently conducting a secondary analysis of the bone outcomes in this trial. In the realm of diabetes, I also lead a meta-analysis examining the efficacy and safety of an inhaled insulin therapy on glycemic control in diabetes. This meta-analysis revealed mild efficacy and some safety concerns.
 - a. Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, Brodsky I, Ceglia L, Chadha C, Chatterjee R, Desouza C, Dolor R, Foreyt J, Fuss P, Ghazi A, Hsia DS, Johnson KC, Kashyap SR, Kim S, LeBlanc ES, Lewis MR, Liao E, Neff LM, Nelson J, O'Neil P, Park J, Peters A, Phillips LS, Pratley R, Raskin P, Rasouli N, Robbins D, Rosen C, Vickery EM, Staten M; D2d Research Group. Vitamin D supplementation and Prevention of Type 2 Diabetes. *N Engl J Med* 2019; 381:520-530. PMCID: PMC6993875
 - b. Ceglia L, Lau J, Pittas AG. Meta-analysis: efficacy and safety of inhaled insulin therapy in adults with diabetes mellitus. Ann Intern Med. 2006 Nov 7;145(9):665-75.
- 4. **Serum Sclerostin:** In collaboration with Dr. Bess Dawson-Hughes, we have conducted secondary analyses of the relationship between serum sclerostin (an inhibitor of osteoblast activity) and season and whether calcium and vitamin D impact serum sclerostin.
 - a. Dawson-Hughes B, Harris SS, **Ceglia L**, Palermo NJ. Serum sclerostin levels vary with season. (2014) *J Clin Endocrinol Metab*, 99(1):E149-52. PMCID: PMC3879665.
 - b. Dawson-Hughes B, Harris SS, **Ceglia L**, Palmero NJ. (2014) Effect of supplemental vitamin D and calcium on serum sclerostin levels. *Eur J Endocrinol*, 170(4):645-50. PMCID: PMC3974734.
- 5. **Measuring Calcium Balance:** -- We have identified simple but accurate methods to measure calcium balance (absorption and excretion) in clinical research. We published the use of dual stable calcium isotopes with a 4-h single serum method to calculate fractional calcium absorption values and found it comparable to the gold standard 24-h urine method. I also published another study on the validity of a 4-h urinary calcium excretion after a standard oral calcium load as a practical index of calcium absorption in healthy older adults on a standard calcium intake.

- a. Ceglia L, Abrams SA, Harris SS, Rasmussen HM, Dallal GE, Dawson-Hughes B. (2010) Evaluation of an inexpensive calcium absorption index in healthy older men and women. *Clin Endocrinol (Oxf)*, 72(1):22-5. PMCID: PMC4431538.
- b. **Ceglia L**, Abrams SA, Harris SS, Rasmussen HM, Dallal GE, Dawson-Hughes B. (2010) A simple serum method to measure of fractional calcium absorption using dual stable isotopes. *Exp Clin Endocrinol Diabetes*,118(9):653-6. PMCID: PMC4640182.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1VqhuQoftewks/bibliography/public/